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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/856,025	09/13/2001	Wing L. Sung	07121.0001U1	2247

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EXAMINER

RAO, MANJUNATH N

ART UNIT	PAPER NUMBER
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1652

DATE MAILED: 07/25/2003

11

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/856,025

Applicant(s)

SUNG ET AL.

Examiner

Manjunath N. Rao, Ph.D.

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 22 April 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-32 is/are pending in the application.
- 4a) Of the above claim(s) 23-28 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-22 and 29-32 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 13 September 2001 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 3, 6. 6) ☐ Other: _____

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DETAILED ACTION

Claims 1-32 are still at issue and are present for examination. Claims 1-22 and 29-32 are now under consideration. Claims 23-28 remain withdrawn from consideration as being drawn to non-elected invention.

Election/Restrictions

Applicant's election of Group I, claims 1-22, 29-32 in Paper No. 10 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Priority

Applicant's claim for domestic priority under 35 U.S.C. 119(e) is acknowledged.

Drawings

Drawings submitted in this application are accepted by the Examiner for examination purposes only.

Sequence Compliance

Applicant is required to comply with the sequence rules by inserting the sequence identification numbers of all sequences recited within the claims and/or specification. It is particularly noted that applicants fail to provide appropriate SEQ ID NO to sequences recited in Figure 1 and on pages 25-27 etc. See particularly 37 CFR 1.821(d).

Claim Rejections - 35 USC § 112

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The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 2, 29 and claims 3-22 and 30-32 which depend from claim 1 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 1 and 29 recite the phrase "characterized in exhibiting". The metes and bounds of the term "characterized" is not clear to the Examiner. Deleting the offending term will overcome this rejection.

Claims 3-6 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 3-6 recite the phrase "characterized by said xylanase". The metes and bounds of the term "characterized" is not clear to the Examiner. Deleting the offending term will overcome this rejection.

Claims 12 and claims 13-22, 30 and 31 which depend from claim 12 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 12 (and claim 17) are drawn to "a modified xylanase comprising a basic amino acid at position 162 or its equivalent". It is not clear to the Examiner as to what applicants mean by the phrase "its equivalent". It is not clear whether the amino acid has to occupy the very same position or whether the modified amino acid has to be chemical equivalent, i.e., if the amino acid at position

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162 was a basic amino acid or a aromatic amino acid, it has to be modified with another basic or aromatic amino acid. Furthermore, Examiner urges applicants to provide an amino acid SEQ ID NO in order for the Examiner to conduct a proper search. Without an amino acid sequence it would be impossible for the Examiner to determine position 162.

Claims 18-22 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 18-22 recite abbreviations for the mutations. For example DS1, DS2, DS4 or DS8. It is not clear to the Examiner as to what applicants mean by the above in the context of the claims. Although the claims are interpreted in light of the specification, i.e., that DS may correspond to "di-sulfide bridges", limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Furthermore it is also not clear whether the numerical value represents the total number of disulfide bridges in the modified xylanase.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-10, 12-17, 29-31 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for 1) an isolated from *Trichoderma reesei* and modified such that the amino acid at position 162 is changed to a histidine and further comprises one disulfide bridge specifically between amino acid at position 110 and 154 (TrX-162H-DS1) having SEQ

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ID NO:56 or an isolated from *Trichoderma reesei* and modified such that the amino acid at position 162 is changed to a histidine and further comprises one disulfide bridge specifically between amino acid at position 108 and 158 (TrX-162H-DS2) having SEQ ID NO:57, or an isolated from *Trichoderma reesei* and modified such that the amino acid at position 162 is changed to a histidine and further comprises two disulfide bridges specifically between amino acid at position 110:154 and 108:158(TrX-162H-DS4) having SEQ ID NO:59 or an isolated from *Trichoderma reesei* comprising one disulfide bridge specifically between amino acid at position 110 and 154 and further comprising amino acid changes as follows N10H, Y27M, N29L, N44D, Q125A, I129E and Q162H (SEQ ID NO unknown), does not reasonably provide enablement for any modified xylanase from any source having any structure and having increased or improved thermostability or its equivalents. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in *In re Wands* (858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)) as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claim(s).

Claims 1-10, 12-17, 29-31 are so broad as to encompass any modified xylanase isolated from any source having the characteristics described herein. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large

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number of xylanases broadly encompassed by the claims. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to the modified nucleotide and encoded amino acid sequence of the xylanases isolated from *T.reesei* as described above. It would require undue experimentation of the skilled artisan to make and use the claimed polypeptides. The specification is limited to teaching use of modified *T.reesei* xylanase but provides no guidance with regard to the making of variants and mutants from all other sources. In view of the great breadth of the claim, amount of experimentation required to make the claimed polypeptides, the lack of guidance, working examples, and unpredictability of the art in predicting function from a polypeptide primary structure (e.g., see Ngo et al. in *The Protein Folding Problem and Tertiary Structure Prediction*, 1994, Merz et al. (ed.), Birkhauser, Boston, MA, pp. 433 and 492-495, Ref: U, Form-892), the claimed invention would require undue experimentation. As such, the specification fails to teach one of ordinary skill how to use the full scope of the polypeptides encompassed by this claim.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art

would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass all modifications and fragments of any xylanase because the specification does not establish: (A) regions of the protein structure which may be modified without effecting xylanase activity; (B) the general tolerance of xylanases to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any xylanase and its any amino acid residue with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including xylanases with an enormous number of amino acid modifications. The scope of the claims must bear a reasonable correlation with the scope of enablement (*In re Fisher*, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of xylanases having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claims 1-22, 29-32 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably

convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1-22, 29-32 are directed to xylanase variants. Claims 1-22, 29-32 are rejected under this section of 35 USC 112 because the claims are directed to a genus of polypeptides including modified polypeptide sequences, that have not been disclosed in the specification. No description has been provided of either the wild type or the modified polypeptide sequences encompassed by the claim. No information, beyond the characterization of the source of the wild type enzyme has been provided by applicants which would indicate that they had possession of the claimed genus of modified polypeptides. The specification does not contain any disclosure of the structure of all the polypeptide sequences derived from said source, including fragments and variants within the scope of the claimed genus. The genus of polypeptides claimed is a large variable genus including peptides which can have a wide variety of structures. Therefore many structurally unrelated polypeptides are encompassed within the scope of these claims. The specification discloses only the source of the claimed genus which is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus. Therefore, one skilled in the art cannot reasonably conclude that applicant had possession of the claimed invention at the time the instant application was filed.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

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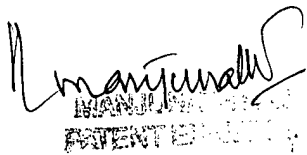
(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-10, 15-16, 29-32 are rejected under 35 U.S.C. 102(b) as being anticipated by Wakarchuk et al. (Prot. Eng., 1994, Vol. 7(11):1379-1386, cited in IDS). This rejection is based upon the public availability of a printed publication. Claims 1-10, 15-16, 29-32 of the instant application are drawn to a family 11, modified xylanase with altered thermostable characteristics wherein the modification comprises disulfide bridges. Wakarchuk et al. disclose that introduction of disulfide bonds in family 11, xylanase isolated from *B.circulans* increases the thermostable characteristics. While the reference does not exactly recite the identical thermostable characteristics as claimed in the instant claims, it does disclose improved thermostable characteristics. Therefore, Examiner takes the position that the modified xylanase disclosed in the reference has the same characteristics claimed in the instant claims as such characteristics can be inherent characteristics. Thus Wakarchuk et al. anticipate claims 1-10, 15-16, 29-32 as written. Since the Office does not have the facilities for examining and comparing applicants' protein with the protein of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed product and the product of the prior art (i.e., that the protein of the prior art does not possess the same material structural and functional characteristics of the claimed protein). See *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *In re Fitzgerald et al.*, 205 USPQ 594.

Conclusion

None of the claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Manjunath Rao whose telephone number is (703) 306-5681. The Examiner can normally be reached on M-F from 7:30 a.m. to 4:00 p.m. If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, P.Achutamurthy, can be reached on (703) 308-3804. The fax number for Official Papers to Technology Center 1600 is (703) 305-3014. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.



MANJUNATH N. RAO
PATENT EXAMINER

Manjunath N. Rao. Ph.D.
July 21, 2003